mosis, gastric resection, or even pancreaticoduodenectomy have been recommended as methods of closure, but with poor results.

Jones[1] reported on a woman who required excision of a 5 cm by 7 cm portion of the wall of the descending duodenum during right colectomy for carcinoma of the colon. Successful repair was effected by retrocolic side-to-side open duodenojejunostomy. This required an open anastomosis, however, with its inherent complications.

Kobold[3] and Wolfman[4] reported a simple serosa-to-serosa closure of experimental duodenal defects in dogs by suturing an intact loop of jejunum over the hole, thereby eliminating the open anastomosis. In their experiments, the serosal surface of the jejunum was gradually covered by duodenal epithelium, the process being complete in four to seven weeks. No anastomotic leaks occurred, and there was no apparent tendency for peptic digestion of the loop.

Jones,[2] working independently, later carried these experiments even further, in that he created a duodenal defect analogous to a perforated duodenal stump, allowing the leak to continue for 20 hours. Then at a second operation the duodenal defect was closed by the "serosal patch" technique. Again, all dogs survived and no anastomotic leaks occurred. This study in infected animals is especially pertinent to the present case report.

With these excellent studies as a stimulus, the first clinical application of the method awaited only the right patient with the right problem. Certainly in the case herein reported it was inconceivable that primary closure of the duodenal defect could succeed, or that resection with end-to-end anastomosis would fare any better. The presence of infection, the poor general condition and immense size of the patient prohibited a major resection. Of course, in retrospect, the pyloroplasty should not have been done at the time of the original operation, and then no fistula would have occurred.

In spite of the Staphylococcal infection and low serum proteins, the postoperative course suggested that the "serosal patch" effectively sealed the defect. At the time of the sudden death of the patient three weeks later, he was eating a soft diet and had no evidence of recurrent fistula. Autopsy showed death due to massive atelectasis and toxic myocarditis. No evidence of anastomotic leak was found.

Additional cases will have to be accumulated and the long-term results studied, but the method gives promise of being a very simple solution to an extremely difficult problem.

Summary

The "serosal patch" technique previously used only experimentally was used in a patient who was in poor general condition and an alcoholic, to close a pyloric fistula resulting from the dehiscence of a Heineke-Mikulicz pyloroplasty done at the time of an emergency poracaval shunt for massive bleeding. Partial evisceration had occurred at the site of incision for the first operation and the wound was grossly infected with Staphylococcus aureus at the time the "serosal patch" operation was done. The patient died in another hospital three weeks later of toxic myocarditis and massive atelectasis, and at autopsy no evidence of anastomotic leak was found.

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Infectious Mononucleosis

With High Heterophile Titer and Neurological Manifestations

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THE DIAGNOSIS of infectious mononucleosis, although the disease may be strongly suspected, usually is not established clinically, until the supporting laboratory tests are secured. These consist of the characteristic "atypical" lymphocytes (virocytes, Downey cells), the elevated heterophile antibody titer for sheep cells (the pre-

From the Department of Laboratories, St. Joseph Hospital, Burbank. Submitted 12 May 1965.

sumptive test), and the differential absorption of these heterophile antibodies by guinea pig kidney and beef heart (Davidsohn differential test). Usually, the heterophile antibody titer is considered presumptive positive at 1:112. Occasionally the titer may be elevated to a ratio of one to several thousand. The highest titer of heterophile antibodies reported in the past 10 years is 1:10,240,[3] but levels of 1:20,000 have been noted.[13] In about 15 per cent of the cases of infectious mononucleosis, titers are found to be below the significant level of 1:112.[5,14,16]

At times, unusual presenting clinical manifestations tend to confuse a definitive diagnosis. The occurrence of an extraordinarily high titer (1:229,376) of the characteristic heterophile sheep cells antibodies in the serum of a patient with severe neurological involvement prompted this report.

Report of a Case

The patient was a 16-year-old white male student who was first seen 1 September 1964 by a pediatrician* because of "sore throat" and temperature of 101°F of two days' duration. A diagnosis of acute follicular tonsillitis was made and antibiotic treatment—benzathine penicillin G (Bicillin) 600,000 U and tetracycline (Acromycin) 100 mg four times a day—and bed rest were prescribed. On 4 September, while walking about at home, the patient began to have difficulty in respiration, became cyanotic and fell to the floor with a convulsive seizure and unconsciousness which lasted approximately five minutes. He was admitted to St. Joseph Hospital by ambulance the same day. The past and family history were noncontributory. There were no previous symptoms of central nervous system disorder.

On examination no outward abnormalities were noted except for enlarged tonsils with prominent crypts filled with purulent exudate. The anterior cervical lymph nodes were moderately enlarged.

At the time of admittance, leukocytes numbered 14,700 per cu mm, of which 66 per cent were lymphocytes. Slightly more than two-thirds of the lymphocytes were atypical, having the characteristic features of Downey cells. The leukocytosis disappeared by the tenth hospital day but significant numbers of abnormal lymphocytes persisted even a month after discharge from the hospital.

The cerebrospinal fluid on the day of admission contained only 3 polymorphonuclear leukocytes per cu mm. The total protein of the fluid was 36 mg per 100 ml and the glucose content, by the oxidase technique, was slightly elevated at 76 mg per 100 ml. Blood glucose was not determined and no colloidal gold or serological tests for syphilis on the spinal fluid were done. On the fifth hospital day the spinal fluid contained 14 leukocytyes per cu mm, all of which were lymphocytes. The protein and glucose content of the fluid was 37 and 71 mg per 100 ml, respectively. Spinal fluid pressure was 160 mm of water.

Episodes of convulsions occurred daily for eight days and were described by the nurses as beginning in the right side of the face. At a later date it was noted that, when the patient was startled, the convulsive seizures began in the right leg. Gordon and Chaddock reflexes were demonstrable in the right foot at this time. With the clinical impression of possible intracranial vascular anomaly, a bilateral carotid angiogram was done on the seventh hospital day. The cerebral vascular pattern was within normal limits. The frequency and intensity of the convulsions, for which diphenylhydantoin (Dilantin®) and phenobarbital were given, diminished progressively during the period of recovery and ceased on the ninth hospital day.

The heterophile antibody titer in the patient's serum on admission was 1:229,376. On the third hospital day, it had dropped to 1:57,344 and after guinea pig kidney absorption it was still positive at a dilution of 1:28,712. No heterophile agglutinins remained in the serum following beef heart absorption.

On the sixth hospital day, leukocytes numbered 4,900 per cu mm, of which 42 per cent were normal lymphocytes, 6 per cent atypical lymphocytes, 11 per cent monocytes and 8 per cent eosinophiles. The heterophile titer was 1:28,712. The patient was discharged 13 days after admission, at which time the heterophile antibody titer had dropped to 1:4,336, the total leukocyte count was 8,200, of which 18 per cent were atypical. One month after discharge, the patient appeared in good health and free of symptoms. Heterophile antibody test was still positive to a titer of 1:448. Leukocytes numbered 9,000 per cu mm, 44 per cent of which were lymphocytes and a third of these were atypical.

*Dr. Wendell Coffelt, whose permission to publish this case is gratefully acknowledged by the authors.

Discussion

Infectious mononucleosis is one of the few systemic diseases that is so protean in clinical manifestations that it mimics many other disease entities. In the case of mononucleosis, this apparently is due to the fact that it is a "generalized systemic disease with cellular infiltration in almost every organ, the clinical picture varying with the predominant site of involvement."[14] For this reason, many of the unusual presenting signs and symptoms are erroneously classified as "complications" although they are in fact different facets of the same disease. The reported incidence of central nervous system involvement in patients with infectious mononucleosis has varied between 1 per cent[1,4,12] and 9 per cent.[6,7] It is said to be more common in males than females, in adults than in children and rare in Negroes. The neurological symptoms usually appear between one and three weeks after the onset of the disease, but occasionally earlier. Many different types of involvement have been reported, most commonly meningoencephalitis, often associated with Guillain-Barré syndrome. Peripheral neuropathy and optic neuritis are less frequent.

The pathogenesis of the central nervous system involvement has not been established but the cause is thought to be direct viral invasion of the brain. The spinal fluid findings are variable.[2] There may be no change, or an increase in total protein and leukocytes, sometimes accompanied by an increase in pressure and an abnormal colloidal gold curve with a midzone rise. The glucose, chloride and serological tests for syphilis are usually normal. The overall mortality rate of infectious mononucleosis is less than 1 per cent, while that of patients with central nervous system complications has been reported at 11 per cent by Nichols and Athreya[11] and as much as 40 per cent by Lawrence.[8] The most common cause of death in patients with central nervous system involvement is respiratory paralysis. Few reports of postmortem studies are available. In a study of 30 cases, Lukes and Cox[10] described foci of myelin degeneration and round cell infiltrates, particularly in the leptomeninges and nerve roots. Erwin[4] also noted such phenomena.

The clinical symptoms, the classical positive serological tests and changes in the peripheral blood established the presence of infectious mononucleosis in the patient reported here. The percutaneous carotid angiograms fairly well excluded the presence of other organic disease in the central nervous system. The onset and resolution of neurological symptoms paralleled the onset and clinical recovery from the infection. This, plus the slight spinal fluid pleocytosis, help establish the relationship between the central nervous system involvement and the infectious mononucleosis.

The most striking finding in this patient was the extremely high heterophile antibody titer—1:229,376, which was doubly checked. It was not until the third day of illness, when the titer had decreased moderately, that the Davidsohn differential test was performed and the type of antibody was found to be characteristic. Similarly high heterophile antibody titers have not been noted in reports of other cases of central nervous system complications. On the contrary, in most such cases the titers were in the low normal, equivocal or slightly elevated range. It would appear, therefore, that there is no direct correlation between the heterophile titer and the severity of the clinical symptoms or the neurological involvement. It is recognized that the heterophile antibody test, first described by Paul and Bunnell in 1932 and later modified by Straus,[16] is a nonspecific or presumptive test for the disease entity. Note is taken of the fact that approximately 15 per cent of the patients with infectious mononucleosis do not have significant heterophile titers.[3,5,16] The unusual response in such cases may be explained by antigenic variability of the infectious agent or by anergy of the patient, phenomena about which more may come to light in the currently emerging concepts of immunogenetics.[17] Some investigators report a very much lower incidence of heterophile-negative patients with infectious mononucleosis,[3,9] but this is due to their acceptance of a lower limit (1:64) as evidence of a positive test. Since a relatively high proportion of normal controls have titers up to 1:112,[15,16] we consider that titer as only presumptive positive and 1:224 as positive. It is interesting to note that in the present case the titer of heterophile antibody remained elevated long after clinical recovery, whereas usually the titer declines to normal with defervescence,[16] although occasionally it may remain elevated for 30 days or more. Another interesting facet of the case here reported is that during the period of recovery the blood eosinophiles increased to 8 per cent, a fact which was considered to be of reassuring prognostic significance. Failure to demonstrate an

increase of serum transaminase levels is evidence against major tissue destruction.

Summary

A 16-year-old boy with severe infectious mononucleosis with signs and symptoms of extensive central nervous system involvement and an unusually high heterophile titer (1:229,376) has been described. Other significant laboratory findings included a slightly increased spinal fluid glucose level and the persistence of an elevated heterophile antibody titer after clinical recovery.

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Esophageal Hiatal Hernia Following Vagotomy

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ESOPHAGEAL hiatal hernia may occur following vagotomy whether or not the esophageal hiatus is found to be dilated at the time of operation, although herniation is more likely if the hiatus is dilated. An asymptomatic esophageal hiatal hernia may become symptomatic following vagotomy. Surgeons should be aware of this when vagotomy is done and tighten the diaphragmatic crura if the esophageal hiatus is found to be dilated after the completion of vagotomy. Esophageal hiatal hernias should be repaired at the time vagotomy is done.

There is very little awareness of this complication following vagotomy. Kearns[1] said that diaphragmatic hernia following vagotomy is extremely rare, and that closing the peritoneum over the hiatus to prevent future herniation is not necessary. (The author is not aware that such a procedure would ever prevent an esophageal hiatal hernia.) Weisel and coworkers[2] described the hazard of associated esophageal hiatal hernia in patients having abdominal operations such as gastrectomy and cholecystectomy. They did not, however, mention vagotomy. The author has been unable to find any case reports of the occurrence of esophageal hiatal hernia after vagotomy.

The following is a report of four cases of esophageal hiatal hernia requiring operative correction following vagotomy, occurring at the Daniel Freeman and Centinela Hospitals, Inglewood, California, in the past 10 years.

Reports of Cases

CASE 1. A 48-year-old white woman had bilateral vagotomy and subtotal gastrectomy on 3 May 1956 for a chronic intractable duodenal ul-

Submitted 8 July 1965.